

In the Specification:

Please amend the specification as shown:

Please delete the paragraph on page 17, line 33 to page 18, line 18 and replace it with the following paragraph:

The following reagents were used. Benzoyl-Ile-Glu-Gly-Arg-p-nitroanilide (SEQ ID NO: 17) (S-2222) was purchased from Helena Laboratories. Dansyl-Glu-Gly-Arg-chloromethyl ketone (DEGR-ck) was obtained from Calbiochem. Phosphatidylcholine, phosphatidylserine, recombinant hirudin, and fatty acid free bovine serum albumin (BSA) were obtained from Sigma Chemical Co. Factor IX and factor VIII deficient plasmas were purchased from George King Biomedicals and aPTT reagent was obtained from Diagnostica Stago. Normal human plasma factor IX (IX_{NP}) and factor X were isolated as described in Bajaj and Birktoft, 1993, *Methods Enzymol.* 222, 96-128, and factor Xa was prepared as described in Bajaj et al., 1981, *Prep. Biochem.* 11, 397-412. Purified human factor XIa, protein C, activated protein C, and α -thrombin (IIa) were purchased from Enzyme Research Laboratories (South Bend, IN). Recombinant human tissue factor of aa 1-243 containing the transmembrane domain was generously provided by Genentech Inc. (South San Francisco, CA) and reconstituted as described in Sabharwal et al., 1995, *J. Biol. Chem.* 270, 15523-15530. Phosphatidylcholine-phosphatidylserine vesicles (75% phosphatidylcholine, 25% phosphatidylserine) were prepared by the method of Husten et al., 1987, *J. Biol. Chem.* 262, 12953-12966 as outlined in Sabharwal et al (*Id.*). Recombinant human factor VIIa was a generous gift of Novo-Nordisk (Copenhagen). Purified human factor VIII was obtained from Dr. Leon Hoyer (American Red Cross, Rockville, MD). The preparation was free of all other coagulation factors and contained human albumin as a stabilizing agent. Purification of a mouse monoclonal antibody (mAb) that inhibits the interaction of

factor IXa with factor VIIIa was as described in Bajaj et al., 1985, *J. Biol. Chem.* 260:11574-11580.

Please delete the paragraph on page 19, lines 11-30 and replace it with the following paragraph:

SDS-polyacrylamide gel electrophoretic analysis of factor IX proteins (Laemmli, 1970, *Nature (London)* 227, 680-685), using a 12% polyacrylamide concentration and Coomassie Brilliant Blue staining, is shown in Fig 1A. Each protein appeared homogenous in this system. γ -carboxyglutamic acid concentration of these proteins was also determined by Commonwealth Biotechnologies, Inc., Richmond, VA. Automated Edman degradation of each factor IX protein (~ 0.5 nmol) was performed using an Applied Biosystems gas phase sequencer. γ -carboxyglutamic acid analysis of each sample was performed by alkaline hydrolysis followed by HPLC analysis. The amount of γ -carboxyglutamic acid was quantitated based upon the 46 residues of Asp and Asn present per mol of factor IX. Plasma factor IX and each recombinant protein had 11.5 to 12.5 γ -carboxyglutamic acid residues per mol. The N-terminal sequence of each protein was also determined. All recombinant proteins revealed a major and a minor N-terminal sequence. The major sequence in each case was Tyr-Asn-Ser-Gly-Lys (SEQ ID NO: 11) and the minor sequence in each case was Thr-Val-Phe. The major sequence corresponds to the sequence of mature protein in plasma, and the minor sequence corresponds to the protein in which the prosequence has not been cleaved (Yoshitake et al., *supra*). The minor sequence was not detected in plasma factor IX and it amounted to less than 5% in each recombinant protein. The relative coagulant activity of each protein was: IX_{NP}, 100% (180 ± 10 units/mg); IX_{WT}, $\sim 90\%$; IX_{L330I}, $\sim 8\%$; IX_{V331A}, $\sim 6\%$; IX_{D332Y}, $\sim 2\%$; IX_{R333L}, $\sim 0.3\%$; IX_{R333Q}, $\sim 0.5\%$; IX_{T335A}, $\sim 40\%$; IX_{L337I}, $\sim 1\%$; IX_{R338Q}, $\sim 65\%$; and IX_{helixVII}, not measurable.

Please delete the paragraph on page 30, lines 30-37 and replace it with the following paragraph:

Factor IX Peptide Competition Assay in the presence of factor VIIIa:

Each reaction contained 0.2 nM factor IXa, 480 nM factor X, 0.07 nM factor VIIIa, various concentrations of peptide, 10 μ M phospholipid, and 5 mM CaCl_2 in TBS (Tris-HCl, pH 7.4) containing 1 mg/mL BSA. Each reaction was incubated for either 30, 60, 90, or 120 seconds and the reaction was stopped by adding 1.5 μ L of 0.5 M EDTA and placed on ice. Forty μ L of each reaction was added to 100 μ L of TBS/BSA in a 96 well microtiter plate and S-2222 (Bz-Ile-Glu(γ -OR)-Gly-Arg-*p*-nitroanilide) (SEQ ID NO: 18) was added to a final concentration of 100 μ M. The change in absorbance at 405 nM was then observed using a Bio Rad microplate reader.

Please delete Table 2 on page 30 and replace it with the following table:

Table 2. Sequence of helix-330 in vitamin K dependent four coagulant and one anticoagulant (Protein C) serine proteases. The sequence of helix-330 is identical in factor IX from human, bovine, porcine, canine, rabbit, sheep, guinea pig, mouse and rat. For comparison, the residue number for each protein corresponding to residue 162 in chymotrypsin is given in parenthesis. A hyphen indicates the same residue as in factor IX. All sequences are taken from Bajaj and Birktoft, 1993, *Methods Enzymol.* 222, 96-128.

Protein	Sequence
Factor IX (330)	[162] L V D R A T C L R [170] <u>(SEQ ID NO: 1)</u>
Factor VII (304)	R L M T Q D - - Q <u>(SEQ ID NO: 12)</u>
Factor X (344)	Y - - - N S - K L <u>(SEQ ID NO: 13)</u>
Prothrombin (487)	I - E - P V - K D <u>(SEQ ID NO: 14)</u>
Protein C (325)	V - P H N E - S E <u>(SEQ ID NO: 15)</u>

Please delete Table 4 on page 31 and replace it with the following table:

Table 4

Peptide	K_d (μ M)
P-4488 SEQ ID NO: 2 (DRAT)	44.9 ± 14
P-4351 SEQ ID NO:5 <u>NO:6</u> (LVDRAT)	0.35 ± 0.1
P-4352 SEQ ID NO:6 <u>NO:7</u> (LVYRAT)	6.6 ± 1.2
P-4353 SEQ ID NO:7 <u>NO:8</u> (LVDQAT)	4.7 ± 1.7
P-4354 SEQ ID NO:8 <u>NO:16</u> (TKVSRYVN)	1.0 ± 0.3
EGF1 Domain	6.0 ± 1.5